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TUBERCULIN AND THE LIVING CELL.

*An Inquiry as to how the One Aids the Other in the Fight
Against Tuberculosis.*

BY

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TUBERCULIN AND THE LIVING CELL.¹

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BY CHARLES DENISON, A.M., M.D.,
OF DENVER, COLORADO.

THE wonderful discovery of the bacillus of tubercle had not been demonstrated a longer time than might be reasonably expected before its consequent—the specific cure of tuberculosis—was, it now appears, too hastily given to the world by the same earnest student of nature, Robert Koch, of Berlin.

The history of these two great discoveries is interesting and familiar to every student of medical progress, and needs no repetition here. But what is most remarkable is the present attitude of the great mass of the medical profession toward this second discovery—tuberculin—now, nearly a year and a half after it was given out for use in America. The failure of distinguished men in the use of the remedy, according to the rules laid down by its discoverer, seems to have led to a feeling almost universally hostile to its employment. Editorial comments in medical journals are sneering and derisive in tone; authors in sections of the American Medical Association refer to the “failure” of tuberculin as a

¹ Read at the Ninth Annual Meeting of the American Climatological Association, held at Richfield Springs, June 22, 23, and 24, 1892.

positive conclusion ; and writers in medical periodicals continue, as of yore, to pronounce the edicts of their own conclusions, that there is no such thing as a specific for tuberculosis.

A few weeks ago an Associated Press dispatch went the rounds that a certain Dr. A. M. Brown had announced in a medical meeting in Cincinnati that Professor Koch had acknowledged to him personally that "tuberculin was a failure." Knowing that the statement must be false, I wrote to Professor Koch, and have just lately received his reply. It gives me great pleasure to be able to refute such a slander of one who is doing so much for his fellow men. Dr. Koch writes me that neither he nor his assistants know Dr. A. M. Brown, of Cincinnati, who, however, like others, may have visited the laboratory. His statement that "much of his time was spent in the laboratory of Professor Koch is false, and when he says that I have told him that tuberculin is a failure he states an impertinent fabrication." Professor Koch goes on to say that he has "the same belief in tuberculin as in the beginning. If it is used in the early stages of tuberculosis it will be highly useful." His experience is that this effect is a cure or "Heilung." "It is essential to discover the disease in time, which is best done with this material. To any one," Koch concludes, "who has ever spoken to me about it, I have never made any different assertion than the foregoing."

To the great majority of persons one of the most convincing modes of argument that can be used with reference to tuberculin is to deride the physician who would give his patient a remedy that he would not take himself. To a logically disposed and naturally suspicious layman this assumptive

argument is conclusive, and the fearful idea seems to find a favorable culture-field, not only among laymen, but among professional men, because of the incomplete knowledge of nature's laws and the undeveloped state of bacteriologic science.

A considerable experience with tuberculin during the past fifteen months, under conditions well calculated to enable one to judge of its peculiar and best effects, warrants me in saying that I would not hesitate to employ the remedy in my own case if I should again find myself tuberculous and be convinced of its need, as I have been convinced in the cases in which I have used it. This so-called "failure" of Koch's lymph has not been essentially in tuberculin, but rather in the inability of the medical mind to comprehend the method and the conditions requisite for its success. Nevertheless, the *receiving* medical practitioner, especially if he be handicapped by incompetency, should not be compelled to bear the blame that belongs chiefly to the *giving* originator of such a theory. Let me here say, that in criticising the rules promulgated when this new method of treatment was given to the medical profession I do not wish even to seem to detract from the renown due the great discoverer. It is glory enough for one man to have illuminated the dark regions of the etiology of tuberculosis, and to have set the medical world thinking and working as has Professor Koch.

However, a different application of Koch's discovery seems to be positively demanded, so that sources of error may be eliminated and a successful line of action be marked out for the largest possible number of medical men.

It was my own belief from the commencement that all of Koch's rules for the use of tuberculin were

tentative, and that only in the crucible of time and experience could it be determined what rules would be confirmed and for what ones substitution must be made. I believe I owe my own success largely to my independent mode of procedure. For instance, I commenced with smaller doses, took more time for the treatment than Koch recommended, opposed the confinement of patients, and insisted on regular and systematic out-door exercise.¹

It is not my intention to detail minutely the physical condition and course of treatment of the forty-eight cases (which include all up to June 1st) in which I have employed tuberculin. A paper on "Tuberculin," read at the last annual meeting of the Colorado State Medical Society, contains a report of my first twenty cases. The results in five of these forty-eight cases properly ought not enter into the final conclusion, for to them tuberculin (from 1 to 5 milligrams) was given only for diagnostic purposes. Two of these five are dead; in them the diagnostic effect of the tuberculin showed the utter uselessness of any effort whatever to check the destructive process. Of the remaining forty-three cases, I know of only four that have died. One of these died of measles a month after the last treatment (mentioned in the previous report referred to).

¹ A suitable method for the recording of temperature, pulse, respiration, etc., by the patient himself was also a part of my plan, together with devising a new antiseptic hypodermatic syringe for giving tuberculin. The latter, Tiemann & Co., of New York, have made for me, having milligrams marked on one side of the barrel and minims on the other, and with an adjustable piston-head, constantly fed with oil from a reservoir in the piston-rod to prevent shrinkage and make it work easily. These, with the individualizing of each patient, and the discovery of the stethoscopic signs of reaction to tuberculin, have proved to be valuable aids to the success of the treatment.

Another case, of laryngeal tuberculosis, with a large cavity in the lung, died four months after a short course. Another died at his Canadian home of extensive involvement of the lungs five or six months after cessation of treatment; and a fourth, much improved, though with considerable excavation, died suddenly with pulmonary hemorrhage a year after taking a partial course.

All of the cases (twenty-three in number) in which the dose of thirty milligrams or over was reached are now living and furnish good illustrations of the value of the treatment. Undoubtedly some of these, as well as others in which the treatment has not been concluded, will sooner or later die of tuberculosis, for already one or two have given up the fight, both as to healthful living and treatment, because of indifference or such natural results as exhaustion or lung-contractions, with circulatory or respiratory embarrassment.

Yet, on the whole, the results have been good enough, especially for the thirteen cases classified as finished or cured, and I cannot see how anyone cognizant of the serious lesions existing could hope for better.

The following table gives a classification of these cases, all having pulmonary tuberculosis; one also had lupus; in all but three the sputum contained bacilli previously to treatment with tuberculin.

TABLE.

Total number of cases	48
Average age at commencement	30½ years.
Number of males	31
Number of females	17
Number in first stage of the disease—infiltration (or bronchial)	15
Number in second stage of the disease—softening (or catarrhal)	3

Number in third stage of the disease—excavation	30
Excavation as large or larger in area than a hen's egg in	13 cases.
Excavation or large bronchiectasis on both sides in	3 "
Excavation, small and on one side, in	17 "
The largest dose of tuberculin (two milligrams or less) was used in	3 "
From 2 to 10 milligrams was reached in	10 "
From 10 to 30 " " " " " " " " " " " " " " " "	12 "
From 30 to 50 " " " " " " " " " " " " " " " "	3 "
From 50 to 100 " " " " " " " " " " " " " " " "	13 "
Over 100 " " " " " " " " " " " " " " " "	7 "
Both lungs were affected in	42 "
Only one lung was affected in	6 "
Uncompleted cases, including some yet under treatment, with good results so far as they have gone	13
Graduated (finished) cases at an average dose of 80 milligrams	13
Average time these were under treatment	3½ months.

The thirty-five unfinished cases, including all of the others, were under treatment for an average length of two months. In ten, the most advanced in treatment of the unfinished cases, the average dose reached was $83\frac{1}{2}$ milligrams; these were under treatment for four months. These ten, with a few cases perhaps wrongly included in the finished list, include the tolerant or partly healed cases with cavities, the dismissal of whom, to my mind, is yet questionable; that is, as to the time when that would be safe. The time when the bacilli will all be cleared out is necessarily uncertain, because some of them are always quite sure to be retained in a cavity beyond the time required for them to multiply. The remainder of the unfinished cases, including those in which tuberculin was used for diagnostic purposes only, twenty-five in number, were under treatment, on an average, over a month; the maximum dose averaged 10 milligrams. There are also included eight or ten

that left off the treatment for various causes (see my former report, referred to, for examples), as well as a number of cases doing well, but still under treatment or taking what I call a midway rest in the course.

In only eight are the results recorded as unfavorable, chiefly on account of physical or diseased conditions. This latter class includes some or all of four diagnostic cases recorded as too acute or too generally infected for treatment with tuberculin. The good general condition of those dismissed previously to six months ago speaks better for the permanency of the effects than I had anticipated. It is an open question yet, however, when a person once tuberculous is absolutely free from taint—that time alone can determine.

Among the important questions to be considered is:

The modus operandi of tuberculin in tuberculous tissues.

In my report on this subject to the Colorado State Medical Society last year, I advanced a theory of the action of tuberculin which I much wish bacteriologists would either refute or more fully elucidate than, so far as I am aware, has yet been done. This theory or explanation was based upon the power of living cells to repair injuries to themselves independently of other parts of our body. This idea not only recognizes the power of the tissues to reproduce their like, but also indicates an independent thought of nature that takes some cognizance of the extent of the injury and the quality of the injuring agent. The directness with which the hypodermatically introduced antitoxine of tuberculosis, or whatever else it is in tuberculin that constitutes its

active principle, goes to the highly susceptible tuberculously affected tissue and there stimulates a healing process, is strongly suggestive, if not proof-positive that there is a natural susceptibility of those affected cells, because they are thus diseased. This effort in the direction of healing is an exaggeration of any attempt at repair previously made—a function involving purpose and selection, not heretofore attributed to the ultimate divisions of the living body.

Histologists do not appear to have yet fully comprehended these functions of the living cell; yet some of us practical physicians are convinced, both by experience and by analogy, of certain specific effects of tuberculin, and invite biologists, histologists, and bacteriologists to explain the facts and physical evidences upon which our conviction is based. Is the demand unreasonable? The histologists can describe, as Richard Garnet, of London, has nicely done, what connective-tissue cells are; how, as nucleated corpuscles, they variously lie in a matrix, through the interstices or minute channels of which granular or wandering cells freely pass, on missions of supposed utility, and in which spaces the lymphatics find their terminal ramifications—all of which suggest an intimate relation between the lymphatic system, the white corpuscles of the blood, and the connective-tissue cells—in other words, the means of repair or the fibrous healing-process. Yet neither this histologist nor any other can tell any better than you or I how the life-principle in these cells enables them to change their form, to increase their number, and to exhibit a power of choice and self-direction of action according to the various demands made upon them, such as is observed in a higher order of living beings.

It may be that this contemplation of the living cell, rather than the great complexity of minute forces—the animal body—will bring us nearer to the desired solution of the mystery of *life*. It is only nearer, however; the goal is not reached. Here in the living cell, followed down to the minutest subdivisions of which a powerful lens will allow us to judge, is *life*, existing separately and independently, as well as in combinations. These associations are either harmonious or in controversy with other microscopic existences. Here, in the region of the living cell, is waged an incessant, many-sided warfare between living *constructive* and equally living *destructive* cells, compared with which, as numbers go, the wars of nations are as nothing; and there is no cessation until either the allotted end of life of all of these cells is reached, or is anticipated by the death of the individual.

As to any difficulty others may have in accepting my explanation of the special action of tuberculin on the living cell, if study and reflection have the same effect upon their minds as they have had upon mine, the operation will grow in simplicity and naturalness. It is quite possible, I will admit, that my own vision is influenced by the *fibroid* glasses through which I am inclined to look in the explanation of nature's choice of the healing process in the arrest of chronic pulmonary phthisis. This view is based upon the observation of nearly 4000 cases under climatic and other conditions, which have shown a greater amount of nature's reparative processes than I believe has been shown by any like collection of similar invalids. Besides, is it not best, if possible, to explain these intricate effects upon natural grounds? For instance, is it

not preferable to hold the theory that the formation of vomicæ in the lungs, of anal fistulæ, of rectal ulcers, etc., in the tuberculous are corrective excreting processes, rather than meaningless diseased foci, not to mention the natural efforts at elimination as indicated by septic chills and fever, odorous perspiration and colliquative diarrhea? We look upon these as the outward expressions of an inward warfare between the myriads of bacilli and the greater or less number of living cells.

The explanation given seems to me to be on the same line with the recent efforts among distinguished German experimenters, Ehrlich, Kitasato, and others, to find in animals a natural opposing element to toxic principles. Their success in fixing upon the juice of the thymus and lymphatic glands as attenuating or neutralizing the toxic principles of typhus, diphtheria, tetanus, etc., is to me a wonderful discovery, not so very unlike that of vaccination for smallpox; yet showing that the animal system is by nature furnished with the means, could we only discover them, to combat "every ill flesh is heir to."

Then if, as is true, the known and appreciated effects of tuberculin in tuberculous tissue, when rightly administered, differ very little from the natural processes of cure to which the profession has all along been trusting, that harmony of action is a good guide to be governed by. Physicians have always tried, and I fear they always will, to assume the credit that rightly belongs to a patient, through an unrecognized *vis medicatrix naturæ*. One cannot intelligently and fairly compare the excellent descriptions of cured lesions in tuberculous lungs, in persons dying of other diseases (so well described in

a paper lately read before the New York Academy of Medicine by Dr. H. P. Loomis), with the known effects of contraction in affected lung-tissue and shrinking of cavities due to the action of tuberculin, and not feel convinced that the two processes are so similar as to be practically alike—a natural method of healing.

For the purpose of a minuter description of the treatment with tuberculin I will divide the effects into three divisions: first, external, at the point of injection; second, general or systemic; third, internal lung-reactions. That no confusion with other kinds of reaction to tuberculin may be possible, I will confine this part of the description to the third division, or the *local effects* in tuberculous lung-tissues, and to the principal physical signs by which they are recognized. I will also separate the third division into three subdivisions: (1) hyperemia, (2) congestion, (3) necrosis. These are not stages, as in the progress of a disease like pneumonia, but different results due either to the size of the dose or to the susceptibility of the patient.

The first effect, that of *hyperemia* of the affected lung-tissue, is to be looked for in cases in which there exists moderate susceptibility, with encapsulated bacilli or slight tuberculous infiltration, or more advanced conditions, if there be a response to very small doses of tuberculin. There is probably an increased flow of blood to the affected part, and also an attraction of leukocytes, as shown in the experiments of T. Mitchell Prudden, who found that when dead bacilli are injected into living tissue, the white blood-cells are attracted in great numbers to the point. The same thing happens if the bacilli are alive, according to Dr. Bennet S. Beach,

of New York. Here is to be found the process of elongation of these attracted cells, and their conversion into connective-tissue elements for the ultimate purpose of strangulating or suffocating the imprisoned bacilli. This is sufficient, if kept up, to do more than simply arrest the tuberculous process. It inaugurates a cure.

The physical signs of this reactionary effect, as I think I was the first to point out in my last year's report, consist mainly in a *harsh, puerile, or an exaggerated broncho-vesicular breath-sound*, as heard with the stethoscope over the affected or reactionary area. This is an exaggeration of what was heard before the tuberculin reaction, or it is heard in localities in which the breath-sound was previously inaudible or entirely different. It is not an evanescent effect, but usually continues, though in a lessened or lessening degree, during the whole course of treatment.

The second division of the reaction to tuberculin, that of local *congestion*, is an exaggeration of the first effect, to the extent of more or less local inflammatory engorgement. The greater swarming of the leukocytes and constructive or defensive cells to the infected areas may be so marked as to somewhat impede the circulation of blood therein, and dyspnea will be caused, with or without an exalted or depressed state of the nervous system, a feverish exhilaration, or perhaps a fear of impending suffocation or harm. Sometimes there is even slight hemoptysis. Now, the process of elimination, under certain conditions, is indicated by the local appearance of moist râles, which more or less obscure the usually dry condition characteristic of the reaction to tuberculin in the affected tissue. It is here that the danger of

reinfection may threaten if these moist râles are found in inefficiently ventilated portions of the lung. If the pyrexia is high, and appears late, especially if it is prolonged at a high point on the following day, the indication of a septic state (which may be the ushering in of a necrotic process in a tuberculous area) is so strong that the greatest caution must be exercised lest the destruction of the most affected spot occur. Previously to this, with or without the advent of moist râles, there is likely to be an increase of expectoration, with increased throwing off of dead or dead and live bacilli. This is followed by a decided lessening of expectoration as well as of the contained bacilli. Percussion does not afford nearly as much information as does auscultation. However, if from imperfect lung-ventilation, with or without the presence of moist râles, an occluded region is made known by an increase of dulness on percussion, an increased resonance is quite sure to follow the opening up of the affected lung afterward, and the appearance of the drying and contracting stage, which is the expected later beneficial effect of tuberculin.

The third and worst effect of tuberculin is *necrosis*, which I claim should always be avoided if possible. The increased number of cells and cell-elements that crowd around the tuberculous nodules, or into and around affected areas, furnish a new, highly inflammatory substance, largely composed of giant or nucleated cells. By the multiplication and breaking down of these the circulation is shut off on the one side, the tuberculous tissue being on the other; the result is death of that tissue or *necrosis*. The enemy and the containing tissue have both been destroyed together in the general shrinkage

and sloughing that have thus been inaugurated. An enormous number of bacilli may then be thrown off in the sputum, which may also contain elastic fibers, shreds of lung-tissue, and pus-cells.

Meantime, nature's effort at repair, if possible, corresponds with the extent of the injury in the affected area, and her process of infiltration and fibrous contraction is inaugurated, which may be the cure of the patient so far as that affected spot is concerned. However, the risk and shock to the individual, the deprivation of breathing-space, or involvement of other tissues, may be too great, and a more conservative and waiting plan of treatment ought to be followed. It should be borne in mind that all three of these degrees of effects may exist at the same time in different parts of the same lung.

The success of treatment with tuberculin rests upon many precautions, or upon favorable conditions to be secured by the physician in charge. Among these are: (1.) The proper selection of cases. (2.) As thorough a knowledge as possible of the physical condition. (3.) The natural resistance of the tissue. (4.) The intensity and extent of the tuberculous infection; and (5.) The gradation of the dose.

The selection of cases suitable for treatment with tuberculin is a most important consideration. It is by exclusion of unfavorable conditions that mistakes are to be avoided. Besides, here in Colorado, I do not think it necessary to subject patients to this additional trouble, anxiety, and expense, who are so slightly affected and otherwise so well suited to the climatic cure, that they are likely to recover anyway. So it happens that I have refused or decided not to employ tuberculin in treatment in probably

twice as many cases as those in which I have employed it.

An important consideration is the ventilation of the affected lung. For, if it is true, as the experimenters state, that in culture-experiments five or six days elapse before tubercle-bacilli begin to be reproduced, then when the bacilli are squeezed or carried out from the tissues into the lung-spaces or bronchial tract they must be removed by expectoration before the expiration of that time, or reinfection will occur. It would be better to leave the bacilli encapsulated than not to get rid of them when they are set free. If the action of tuberculin is expected to take place around the root of the lung or large bronchial tubes, the regions beyond may become convenient receptacles for the infectious tuberculous exudates, when the contracting or healing-process occurs in response to tuberculin. Thus, this question of lung-ventilation is, to my mind, second to no other, and it is a consideration that, it will be acknowledged, gives a great advantage to us who practise in Colorado, where the air is from a sixth to a third rarified.

Now, the question of ventilation, together with the extent and nature of the infection and its results, fibroid or otherwise, can be so well determined that a thorough diagnostician can have confidence in his decisions as to the use of tuberculin. In addition to the usual proofs of a careful physical examination, strengthened by the clinical history of the case and the microscopic examination of the sputum, much direct information is to be gained by the use of the spirometer and manometer, in conjunction with the measurements of the respiratory movements of the right and left sides of the thorax respectively. The

manometer gives the air-pressure that the air-cells will stand, and in a measure indicates the elastic tension, or amount of fibroid or connective-tissue healing that exists; while the spirometer tells the actual capacity of the lungs, which ought to be nearly in an inverse ratio to the amount of fibroid deposit, and also to the extent of the usually accompanying pleuritic adhesions. The rule that I have formulated for determining the respective ventilations of the two lungs (right and left), and which I always mentally follow in my own examinations, is as follows:

Suppose the normal spirometric record of a patient is only one-half of what it should be for his height, and the expansions of the two sides are as one to two, then, if no defect or disease is noted in the better lung, it is well to assume that the lack of ventilation in the other lung is almost complete—that is, the half that is done is nearly all due to the good lung. For other variations in the bilateral measurements this rule can be correspondingly altered.

When it happens, as a result of the reaction to tuberculin, that the ventilation of a lung is defective, then, besides temporarily discontinuing the injections, there are mechanical means that will be sufficient to open up and clear out the suffocated regions. Among these are the use of the lung-compressor or emphysema jacket,¹ the pneumatic cabinet, massage of the chest, horse-back riding, and systematic arm-exercise in the open air. I do not fear the result

¹ This is an instrument I have lately devised for promoting the elasticity in overstretched and suffocated air spaces, which, with my own spirometer and a new manometer, that I have lately completed, Messrs. Truax, Greene & Co., of Chicago, are preparing to put on the market.

of this advice to take moderate and systematic exercise, for I have previously taken the precaution in these cases to determine that nature has already commenced, through the fibroid process, to strengthen the affected tissues; and I have always refused (except for diagnostic purposes) to give tuberculin, unless the patient could come to my office. I long ago gave up the idea of keeping these patients penned up in a single building or sanitarium, as has been the custom in Germany. In Denver they spend much of the time on the splendid system of rapid transit lines that radiate in all directions to the suburbs, and some have lived in adjoining towns, and come to the city for treatment from every two to five days, as directed. I am aware that in emphasizing the importance of exercise I am liable to clash with the views of many members of this society. Several papers have been read the tone of which seems to me unnecessarily fearful of the results of exercise. A discussion of the question of *Rest in the Treatment of Consumption*, at Colorado Springs, reported not long since in the *Climatologist*, appeared to be so one-sided as to give the impression that there was no opposition whatever among that excellent group of physicians to such a stand-still policy. In the use of tuberculin it will never do. I would rather run the risk of over-action, or even hemorrhage from exercise, than, because of the lack of it, allow the dead or live bacilli to remain and reinfect the system.

Another important point to decide before commencing injections of tuberculin is that there exists *only* the fever of tuberculosis, and not, in addition, the septic-pyemic fever that attends the breaking-down of lung-tissue and the extensive

caseation of tubercles. There is no reason to expect tuberculin to do any good in this second form of fever, but, on the contrary, aggravation of the previously existing septic state might naturally be expected, for, as Klebs, of Zurich, in a letter lately received, expresses it: "You will also have fever by the introduction of pyrogenic substances from out the destroyed bacilli; but this fever is very well supported, and will cease if all or the greater number of the bacilli are destroyed." The want of an appreciation of this fact may be at the bottom of the fear that so largely pervades the medical mind—*i. e.*, a suspicion that tuberculin contains proteid substances that will themselves cause the septic fever.

I believe that this fear is unwarranted, and springs from the non-recognition of the previously existing septic state; in other words, tuberculin is a better diagnostician than its too suspicious professional critic. The natural result of this state of affairs is the demand that an effort be made to eliminate these harmful ingredients, supposed to be contained in tuberculin. Consequently, the chemistry of the extract is minutely gone into, and, according to Klebs, by treating it with platinum chloride, and filtering through alcohol, the alkaloid and harmful ingredients are thought to be separated, and the albuminoids, supposed to contain all of the active healing principle, are saved, and finally constitute two and a half per cent. of the original tuberculin. I have not yet used any of this "tuberculocidin" of Klebs, nor Hunter's similar modification of tuberculin, for I do not need them, as I do not hold the same belief as they do as to the necessity of their procedures, and further, because I have a better guide than the usual fever-range in the

stethoscopic signs of reaction to tuberculin. Besides, Klebs's results with his tuberculocidin are no better than, if as good as, my own with tuberculin.

Dr. Libbertz writes me that tuberculin has been made constantly uniform since the beginning. Though the results in Dr. Kinnicut's¹ cases, treated with Hunter's modification, were in the main favorable, I can make no use of them, because a constant stated dose was given at regular intervals, which is quite different from my plan—*i. e.*, the gradually increasing dosage for a given desired effect. I wish that we knew more about the composition of tuberculin and the chemistry of these substances proposed as substitutes. As the case now stands, I am rather inclined to agree with Koch, who says that much of the active principle of tuberculin goes through the dialyzer in making Hunter's modification, and, therefore, I conclude that both Hunter and Klebs are using a much diluted tuberculin, just as they ought to do anyway.

Dr. Klebs claims that his tuberculocidin has an effect additional to that of tuberculin, in that it kills the tubercle-bacilli. The claim cannot be allowed, because others (Dr. Beach, of New York, for instance) have found the same destroying influence to belong to tuberculin, the proportion of the dead bacilli thrown off in sputum being variously estimated up to over 80 per cent. of the whole number. If Koch's extract exerts an injurious septic influence, certainly a patient of mine who has taken the injections for more than a year ought to have shown it by this time. This is a case of laryngeal tuberculosis in the third stage, fully reported in the *University*

¹ New York Medical Record, May 21, 1892.

Medical Magazine for March, 1892. I gave him 180 milligrams on the Sunday before I left home. He always asks for a large dose as he comes on his weekly visit, saying that he feels better if he perceives some appreciable effect of the injection.

After all, perhaps, it is not strange that a fear of the consequences should generally exist among medical men, when we consider that the destructive process of pus-formation and the constructive process of repair—connective-tissue growth—are so near each other, both originating in different degrees of inflammation under varying conditions. This thought grows in importance if it be considered that tuberculin, if given as Koch first directed, to produce necrosis, may favor this destructive process—as it will if given in too large doses, while, if given in smaller and appropriate doses, the effect will be constructive, with a return to a state of health.

The influence that tuberculin may have upon these processes is most interesting. The question has been raised by Prof. W. T. Councilman¹ whether or not the fibrinous exudation in the alveoli around the tubercle or in its neighborhood is a part of the tuberculous process? He considers that it is, because bacilli are found in this contiguous inflammatory tissue. Why should we not rather look at it as the natural reparative process excited by the central tuberculosis, the purpose of the fibroid process being the limitation of this destructive tendency? At the same time we will admit that the extension of tuberculous infection may be temporarily favored by the stasis of blood in this border-ground of the

¹ Article on "Tuberculosis," in Reference Handbook of the Medical Sciences.

contest that is going on. In tubercles with centers undergoing caseation the fibrous tissue seems to be antagonistic to caseation—*i. e.*, the more there is of the one, the less there is of the other; sometimes a caseous mass resulting, and sometimes a fibrous nodule with a shrivelled nucleus at its center. In these nodules Cornil and Ranvier found bloodvessels, and rightly reasoned that in them, and not in the caseous nodules without vessels, the cells retain their vitality to resist the tuberculous process. Is it not quite possible that tuberculin acts as a special stimulant to these fighting cells, and that the decidedly diagnostic sign of the commencing fibroid process under treatment with tuberculin is proof that both blood-circulation and connective-tissue formation are advancing into the lines of the enemy—*i. e.*, the tuberculous stronghold?

Councilman says that the tubercle-bacilli are taken into the tissues from the communicating air-spaces by the white corpuscles, and Koch also claims that these white corpuscles are changed into epithelioid cells by the action of the bacilli contained in them. If this is so, why is it not reasonable to infer that the process of cure is the reverse of the foregoing—*i. e.*, that the contracting influence under the reactions of tuberculin leads to the breaking up and subdivision of these giant and epithelioid cells? These, the natural homes or protecting envelops of the bacilli, after subdivision and still bearing their bacilli with them, become the exudative cells, which sometimes crowd the air-spaces in the region, presenting a local reaction to tuberculin. I have noticed that this connective-tissue increase, the most prominent feature of the healing process that takes place in connection with

the employment of tuberculin, is likely to be accompanied with or preceded by an increase in this exudation. Does it not appear reasonable that this stage in the effect of tuberculin should be known and watched by the attending physician with the greatest care and caution!

Dr. Armand Ruffer, of the British Institute of Preventive Medicine, has lately asserted that it is the poisons excreted in the tissues by infectious microorganisms that attract the leukocytes to battle with the germs, and that the reason that in certain virulent cases this attraction is lost and the work of the defending leukocytes is ineffectual or feeble, is that these toxic principles are too generally distributed in the system—*i. e.*, in the blood-current, as well as localized in the tissues. Dr. Sternberg, of the U. S. Army, calls attention to the fact that Tizzoni and Centanni, experimenting upon infected guinea-pigs with Koch's lymph, stated that recovery is due to the development of an antitoxine that neutralizes the tuberculous virus. They seem to conclude that the antitoxine is developed in the tissues in consequence of the injection. Whether this is so, or if the antitoxine already exists in the tuberculin, as it is more reasonable to believe, further observation will have to decide. The influence is certainly specific upon tuberculous tissue. I could illustrate this by showing the gradual shrinkage of tuberculous glands on the side of the neck in a young woman among the unfinished cases in my list.

I have conceived the idea that perhaps the nodules that we have been accustomed to call tubercles are simply nature's prison-vaults for the incarceration of the offensive bacilli; and, until someone proves the contrary, I shall not cease to suspect that the

bacilli, when thus imprisoned, are deprived of nutriment for growth, or, perhaps, by pressure are prevented from multiplying, and that this perfected imprisonment constitutes the completeness of the state of "arrest" of pulmonary tuberculosis, whether by climate or otherwise, as heretofore accepted by the medical profession. Even more, the *policeman* function of the leukocytes, "the free lances of the body," may yet be shown to include the arrest of these bacillary intruders and detention within their own bodies until, having the power to do so, they can call to their aid those constructive and repairing carpenters—the connective-tissue cells—to build about themselves and their captured bacilli the strongholds intended for their permanent imprisonment.

If the foregoing figure is a reasonable representation of this inward struggle constantly going on in many of the human race, how very like a punishment for any future sins of omission or commission on the part of the tuberculous patient, as to the laws of healthful living, is the escape and multiplication in the body of these convict bacilli when once the resistance of the tissues is relaxed from lack of nutrition or nerve-support.

The difference is so great between tuberculosis in arrest, with the natural resistance of the tissues everywhere able to maintain their integrity, and tuberculosis of the lungs under full headway, with the living cells deprived of their power of successful resistance, as only to be faintly imagined by one thinking of the computations of bacteriologists. They compute that in this latter condition over twenty-one million bacilli are thrown off in the sputum of an individual each twenty-four hours, or

fifteen thousand per minute. I do not know enough of the methods of division or growth of these germs to compute how many millions of bacilli yet remain in such a body, but this I do know, that that remedy must be a true specific for tuberculosis which bids so fair as tuberculin does to forestall such havoc, and not only aids in the arrest of the tuberculosis, but also supports the living cell in the supreme effort to eradicate the cause from the body. In view of the comparative failure of the usual internal antiseptic treatment of pulmonary tuberculosis by trying to saturate the system with supposed blood-purifiers, or the endeavors to reach the enemy by the use of germicidal inhalants, the physician of the future must come to the rescue of the living cell. In its fight against tuberculosis he will find, in rightly selected cases, the *antitoxine of tuberculin* an unrivalled aid to the best combination of climatic attributes, with sunshine, elevation, and dryness in the foreground, so that with every other attainable aid added, integrity and health may be preserved to the living cell.

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